FRED HUTCHINSON CANCER RESEARCH CENTER

Institutional Review Board

Continuation Review Report

Date:	06/06/2012	**IR file#**	3467-EXT	*This box is for IRO only*	
Protocol#:		**Version date** *(if applicable)*		**Review by Date:** 7/6/12	IRO REC'D JUN 06 2012 **Date Received:**
Principal Investigator:	Garnet Anderson	**Mailstop:**	M3-A410	**Phone:**	4699
Contact Person:	Doris Nodtvedt	**Mailstop:**	M3-A410	**Phone:**	6893
Study Title:	Clinical Coordinating Center for the WHI Extension				

CURRENT STATUS

Indicate the current status of the research:

- ☒ Open to Accrual of new participants; or, for specimen/data only research, the collection of new specimens or records is ongoing.
- ☐ Closed to Accrual – clinical interventions, surveys, or similar participant interactions continuing.
- ☐ Closed to Accrual – remaining activity limited to collection of participant long-term follow data.
- ☐ Closed to Accrual - remaining activities limited to analysis of specimens/data already collected.
- ☐ Closed.

Has the status of the study changed since your last Continuing Review Report (CRR)?

- ☐ Yes
- ☒ No

Proceed to Section 1 - General Information

This box is for IRO only

Committee (Reg ID): ☐ A (21) ☑ B (022) ☐ C (5619) Expires 12-12-2014

Assurance #: FWA00001920 Expires 05-06-2014

Agenda Date: 07/25/12

☐ Full Review ☒ Expedited

Approval Signature, Chair or Designee	Date	Printed Name
	7/5/2012	DAVID MALONEY, M.D., Ph.D.

Dates of IRB Approval: 07/05/12 **to:** 07/04/13

****VALID ONLY AS LONG AS APPROVED PROCEDURES ARE FOLLOWED****

DISTRIBUTION: ORIGINAL – IR File COPIES to: Investigator, Contact Person

1.0 GENERAL INFORMATION

1.1 Please provide a summary of your progress with this research to date, including any interim findings and benefits experienced by research participants since your last Continuation Review Report (CRR).

See list of current WHI Publications and abstracts attached

1.2 Please provide a brief summary of any new literature published in the last year that is relevant to this research.

Much information exists from studies researching hormone therapy and their alternatives, cardiovascular issues, chronic disease, supplements, and diet, but the number of participants and data in those studies is generally smaller compared to the Women's Health Initiative. See the list of current WHI manuscripts and abstracts attached.

1.3 Are you requesting closure of this research? (i.e., accrual complete and no further treatment intervention, follow-up, or data analysis required; and no problems since your last CRR)

☒ No

☐ Yes → **please proceed to Section 5; no further information is needed**

1.4 Have there been any changes in the research, new risk information, or any other new information since your last CRR which would alter the following presumptions about the research?

- Risks to participants in this research project are minimized
- Risks to participants are reasonable in relation to the anticipated benefits to the participant or importance of the generalizable knowledge expected as a result of this research.
- The selection of participants, specimens, or data is equitable.
- Provisions for obtaining and documenting informed consent are adequate.
- Appropriate data monitoring is in place to ensure safety of participants.
- Appropriate safeguards are in place to protect participants privacy and confidentiality.
- Appropriate safeguards are in place to protect participants who may be vulnerable to coercion or undue influence.

☒ No

☐ Yes, please explain →

1.5 Have all members of the research team received the required training on Human Subject Protections and if applicable Good Clinical Practices (GCP) per *IRB Policy 2.20 Training* ?

☒ Yes

☐ No, please explain →

Note: If any new members join the research team, the PI is responsible for ensuring everyone receives and maintains required training.

1.6 Are you, or members of your research team, conducting or coordinating study activities at locations outside the FHCRC/UW/Seattle Children's consortium; or have all locations outside the consortium closed since your last CRR?

☐ No

☒ Yes → please submit a *Multi-Center Supplement* along with this *CRR*.

1.7 Is this research activity funded?

☐ No, please explain → _____

☒ Yes → please submit a *Funding Source Supplement* along with this CRR

1.8 **Conflict of Interest**

1.8.a Is this study supported by an FHCRC or University of Washington budget or otherwise financed by FHCRC or the University of Washington?

☐ No → go to Question 1.9

☒ Yes → Check all that apply and complete accordingly:

☐ **University of Washington budget provides support for the study:** Have there been any changes since your last CRR in the financial interest(s) for any members of the research team?
- ☐ No → go to Question 1.9
- ☐ Yes → provide a copy of the letter you received from the UW Office of Research regarding the conflict management plan and go to Question 1.9

☒ **FHCRC budget provides support for the study:** Please respond to Question 1.8.b. Please refer to the Instructions at http://centernet.fhcrc.org/CN/depts/iro/irb/forms/prot-p2-instructions.pdf for definitions of capitalized terms used throughout section 1.8.b.

1.8.b Do you, or any other Key Personnel participating in the Human Subjects Research portion of this study have a Conflict of Interest related to the research?

☒ No → go to Question 1.9

☐ Yes → has the Center conducted a review of this Conflict of Interest?
The Center's Policy and Guidelines or Involvement with Outside Interests is available at https://centernet.fhcrc.org/CN/center_policies/general_counsel/involvement_with_outside_interests.html

- ☐ No → please contact the Office of the General Counsel at (206) 667-1224. Go to Question 1.9
- ☐ Yes → has this review resulted in a finding that this individual(S) has a Significant or Prohibited Financial Interest that limits his/her ability to participate in the Human Subjects Research described in this study?
  - ☐ No → please explain: _____ Go to Question 1.9
  - ☐ Yes → please submit a confirmation from the Office of the General Counsel that a conflict management plan has been approved by the Center Director or designee in accordance with FHCRC Policy. Does the **conflict management plan require disclosure** in the consent for this protocol?
    - ☐ No
    - ☐ Yes → please explain: _____

1.9 Have you completed gathering your research data/specimens and all remaining research activities are limited to analysis of the existing data/specimens? *If your research involves the ongoing maintenance of a repository of data/specimens for purposes of sharing the data/specimens with other research projects you must answer "no" to question 1.9 and complete the remainder of the CRR.*

☒ No

☐ Yes → **Please proceed to Section 5; no further information is needed.**

Note: If the research was originally approved via expedited review category 1 through 7 the CRR will be reviewed under the same expedited category. If the research project was originally approved via full review this CRR will be reviewed under expedited review category 8(a).

1.10 Will this CRR likely qualify for expedited review?

☐ No

☒ Yes → please provide reason by checking the appropriate box below:

- ☒ Previously approved via expedited review (category 1-7).
- ☐ Full IRB determined future CRRs could be expedited (category 9).
- ☐ Remaining research activity is limited to long-term follow-up (category 8a).
- ☐ Other → please explain:

Continue with this CRR and submit an *Expedited Review Checklist for Minimal Risk Activity*

2.0 ONGOING RESEARCH

2.1 Please provide a brief overview of the research **or** reference the specific page(s) of the protocol if applicable:

2.1.a Objectives

The WHI Extension Study 2 follows consenting participants (approximately 93,512) from the last Extension study that initially consented during the original Clinical Trial/Observational study. Primary Objectives of the WHI Extension Study 2 are: Continued active follow-up of HT trial participants to permit estimation of longer term effects of 5 years of HT use on these important clinical outcomes, maintenance of scientific productivity in the area of Cardiovascular Disease (CVD), to describe the effects of the original WHI interventions on rarer clinical events for which the original study was underpowered to address during the initial phase, to continue to describe the experience of women in the HT trials after cessation of study pills and to assess their use of HT or other preparations for menopausal symptoms and osteoporosis prevention and treatment, to continue to enhance the WHI resource and its utilization by collecting and analyzing clinical outcome data and selected additional exposure data over the time period 2011 – 2015 (2016 for the Coordinating Center), to study factors leading to increased risk of CVD in older women of diverse race and ethnicity i.e. CHD, stroke, HF, AF, PAD and VTE), to study what factors determine absence of CVD as part of successful aging, to facilitate ancillary studies, consortium studies, and clinical trials requiring large numbers of clinical outcomes, to mentor and train new investigators, to increase collaborations, and to make data and biologic resources widely available. In 2011 we began implementing the Long Life Study to a max of 8,000 elderly Medical Cohort participants over a 12 to 18 month period, including an in-person home visit to obtain blood and data similar to what was collected at WHI baseline. By obtaining plasma, serum, RBSCs, DNA, and RNA samples, WHI will be poised to support longitudinal ancillary studies of aging and associated health and disease.

2.1.b Inclusion criteria

Approximately 93,512 participants have been recruited in the WHI Extension 2 Study from the 115,000+ Extension 1 Study participants, initially consented in the WHI Clinical Trial/Observational Study. Participants for the Long Life Study are current WHI participants and members of the Medical Records Cohort, comprised of former WHI Hormone Trial participants and African American and Hispanic participants.

2.1.c Exclusion criteria

Participants not part of the WHI CT/OS, dead, or marked absolutely 'no contact' have been excluded.

2.2 Were any modifications to this research submitted since your last CRR?

☐ No

☒ Yes → please provide or attach a list of each approved modification since the last CRR:

IRB Approval Date	**Short Description**
See Attachment A	

2.3 Are you submitting new modifications with this CRR?

☐ No

☒ Yes → please submit a *Research Modification Form* along with this CRR.

2.4 Have any significant new findings, new risk information or other new information become available since your last CRR which may change participant's willingness to continue in the research, or changes the risk-benefit assessment for current and future research participants?

☒ No → go to Question 2.5

☐ Yes → please describe the new information (submit supporting documents as necessary) and respond to Question 2.4.a

2.4.a How have you communicated the new information to participants currently enrolled in the research?

☐ Consent form was updated and all current participants re-consented.

☐ Consent updated for future participants; current participants told of new information with a note in their research record.

☐ Consent updated for future participants; no active participants at the time consent was updated.

☐ NA – research does not involve consenting participants.

☐ Current participants have not been informed → explain why not, including discussion of why the new information does not need to be communicated to existing participants:

2.5 Risk Assessment and Monitoring

2.5.a Is this a biomedical/intervention study or a study involving invasive procedures to research participants?

☒ No → go to Question 2.5.h.

☐ Yes → please respond to Questions 2.5.b. – 2.5.k.

2.5.b Have there been any individual biomedical Adverse Events (AEs) since your last CRR that were related to the research and were (1) unexpected and (2) related or possibly related and (3) serious or suggests that the research places research participants or others at a greater risk of physical or psychological harm than was previously known or recognized?

☐ No

☐ Yes → list with brief description and provide date reported to IRB as an Unanticipated Problem Involving Risk to Participants or Others:

2.5.c In accordance with the data safety monitoring plan outlined in your protocol, provide a very brief summary of all biomedical AEs since study inception that did not individually require expedited reporting to the IRB as an Unanticipated Problem Involving Risk to Subjects or Others.

2.5.d Did the incidents in any category of biomedical AEs outlined in 2.5.c. occur at greater frequency or severity than expected as written in the protocol?

☐ No

☐ Yes → please explain:

2.5.e Have there been any deaths of study participants (for any cause) since the study's inception?

☐ No

☐ Yes → specify the number of deaths and the apparent cause of each. Indicate whether the death was related or unrelated to the study product, treatment or procedure:

☐ Unknown → please explain:

2.5.f Does the research involve an independent safety monitoring committee or a Data Safety Monitoring Board (DSMB)?

☐ No

☐ Yes → please respond to 2.5.f.i. and 2.5.f.ii.

2.5.f.i How often does the independent safety monitoring committee or DSMB meet?

2.5.f.ii Was a review(s) conducted by the independent safety monitoring committee or DSMB since your last CRR?

☐ No → please indicate when the next review will occur: _____

☐ Yes → please submit a copy of the most recent report(s)/minutes.

☐ NA → please explain: _____

2.5.g Is this research reviewed by the Cancer Consortium's Protocol Data Monitoring Committee (PDMC)?

☐ No

☐ Yes → please submit a copy of most recent PDMC minutes.

2.5.h 3rd Party Safety Reports

Have there been any 3rd Party Safety Reports of events from other locations or sources since your last CRR where the event was (1) unexpected and (2) related or possibly related and (3) serious or suggests that the research places research participants or others at a greater risk of physical or psychological harm than was previously known or recognized?

☒ No

☐ Yes → please list with brief description and date reported to IRB as an Unanticipated Problem Involving Risk to Participants or Others:

_____

_____

2.5.i Have any participants experienced unauthorized or unreasonable privacy intrusions in the current approval period?

☒ No

☐ Yes → please explain additional safeguards or controls that have been put in place to avoid similar occurrences in the future and provide date reported to IRB as an Unanticipated Problem Involving Risk to Participants or Others.

_____

_____

2.5.j Have any breaches of confidentiality occurred in the current approval period?

☒ No

☐ Yes → explain additional safeguards or controls that have been put in place to avoid similar occurrences in the future and provide date reported to IRB as an Unanticipated Problem Involving Risk to Participants or Others.

_____

_____

2.5.k Other Unanticipated Problems involving risk to participants or others:

Have there been any non-biomedical events since your last CRR that were (1) unexpected and (2) related or possibly related and (3) serious or suggest that the research places participants or others at a greater risk of physical or psychological harm than was previously known or recognized (e.g., breach of confidentiality, loss of key personnel that will impact completion of the research, issues with the data that will impact the integrity of the research data, etc)?

☒ No

☐ Yes → list with brief description and date reported to IRB as an Unanticipated Problem Involving Risk to Participants or Others:

2.6 Have there been any noncompliance events submitted to the IRB as serious or continuing noncompliance since your last CRR?

☒ No

☐ Yes → list with brief description and date reported to IRB as Serious or Continuing Noncompliance:

2.7 Has there been an accumulation of minor noncompliance events since the study's inception that while not serious, may show a pattern of behavior that if unaddressed may jeopardize the rights and welfare of research participants?

☒ No

☐ Yes → submit an *Expedited Reporting Form for Unanticipated Problems or Noncompliance* along with this *CRR* to report the continuing non-compliance.

2.8 Have any monitors or auditors raised any concerns about your study that required a report from you to the IRB, FDA, or other regulatory agencies since your last CRR? These may include Form FDA 483; sponsor, industry, or institutional monitoring findings; or other findings from external reviews of this study.

☒ No → go to Question 2.9

☐ Yes → please respond to Question 2.8.a

2.8.a Have these reports been submitted to the IRB?

☐ Yes → Please list the dates of the report and when they were provided to the IRB:

☐ No → Please submit a copy of the report, or summary of the issue, and your corrective action plan.

2.9 Have any accrued research participants completely discontinued their participation in the research study since your last CRR (e.g., withdrawals)?

☒ No

☐ Yes → please describe the number of withdrawals and cause for each:

2.10 Have there been any unexpected/unusual negative responses or complaints associated with participant contact or study participation since your last CRR? Examples might include angry letters/phone calls or threats of legal action.

☒ No

☐ Yes → please describe the complaints and their resolution:

2.11 Does this research involve the ongoing maintenance of a repository of specimens or data for purposes of sharing with other research projects?

☒ No → go to Question 2.12

☐ Yes → please submit a current *Repository Supplement* along with this CRR and respond to question 2.11.a:

2.11.a Has the repository released specimens or data since your last CRR?

☐ No

☐ Yes → please complete the table below for all new research projects receiving specimens or data from your repository since your last CRR. Include a copy of the signed confidentiality pledge from each Investigator accessing the repository, registry, or data bank.

IRB # (if FHCRC) or study #	Name of Principal Investigator	Name of Outside Institution	Brief Description of Study's Objective(s)

2.12 Is the research currently open to accrual, or has it been open to accrual at any time since your last CRR?

☐ No → **please proceed to Section 4**

☒ Yes → please continue with the remaining questions in this CRR

3.0 ACCRUAL

3.1 Accrual Table:

- For a multi-center study, both local and total accrual numbers must be provided.
- If this study does not involve multiple sites, complete only the local accrual rows.

	Study's Targeted Accrual Goals	Accrual To Date	Projected Accrual for Last Approval Period	Actual Accrual for Last Approval Period	Projected Accrual for Next Approval Period
Locally	N/A	4547	N/A		N/A
Study-wide	N/A	93,567	N/A	61	N/A

3.1.a Has the accrual of participants been substantially lower than anticipated since your last CRR?

☒ No

☐ Yes → please describe why enrollment is lower than expected, your plans to improve accrual, and how low enrollment will affect your ability to complete the study's research objectives.

3.2 Ethnic, Racial and Gender Accrual Table

3.2.a Complete table below and respond to Question 3.2.b.

- For a multi-center study, both local and total accrual numbers must be provided.

- If this study does not involve multiple sites, complete only the local accrual grid.

CURRENT ENROLLMENT LOCALLY: Number of Participants (*must provide exact numbers—i.e., no ranges*)				
Ethnic Categories	**Sex/Gender**			
	Females	**Males**	**Sex/Gender Unknown or Not Reported**	**Total**
Hispanic or Latino	239	N/A	N/A	239
Not Hispanic or Latino	4,304	N/A	N/A	4,304
Unknown (individuals not reporting ethnicity)	8	N/A	N/A	8
Ethnic Categories: Total of All Participants*	4,551	N/A	N/A	4,551
Racial Categories				
American Indian/Alaska Native	25	N/A	N/A	25
Asian	86	N/A	N/A	86
Native Hawaiian or Other Pacific Islander	See Asian	N/A	N/A	See Asian
Black or African American	90	N/A	N/A	90
White	4,048	N/A	N/A	4,048
More Than One Race	unknown	N/A	N/A	unknown
Unknown or Not Reported	302	N/A	N/A	302
Racial Categories: Total of All Participants *	4,551	N/A	N/A	4,551

*These totals must agree to local data in section 3.1 above

Comments: →

CURRENT ENROLLMENT STUDY-WIDE: Number of Participants (*must provide exact numbers—i.e., no ranges*)				
Ethnic Categories	**Sex/Gender**			
	Females	**Males**	**Sex/Gender Unknown or Not Reported**	**Total**
Hispanic or Latino	2,471	N/A	N/A	2471
Not Hispanic or Latino	89,984	N/A	N/A	89,984
Unknown (individuals not reporting ethnicity)	1,102	N/A	N/A	1,102
Ethnic Categories: Total of All Participants*	93,557	N/A	N/A	93,557
Racial Categories				
American Indian/Alaska Native	317	N/A	N/A	317
Asian	1,880	N/A	N/A	1,880
Native Hawaiian or Other Pacific Islander	See Asian	N/A	N/A	See Asian
Black or African American	6,134	N/A	N/A	6,134
White	81,653	N/A	N/A	81,653
More Than One Race	unknown	N/A	N/A	unknown
Unknown or Not Reported	3,573	N/A	N/A	3,573
Racial Categories: Total of All Participants *	93,557	N/A	N/A	93,557

*These totals must agree to Study Wide data in section 3.1 above

Comments: →

3.2.b. Is your study on track to meet anticipated ethnicity, race and gender goals since the initial application to present?

☒ Yes

☐ No → Describe your plans to meet the anticipated accrual goals in relation to ethnicity, race and gender for this current approval period.

☐ NA → Information is not available; explain.

4.0 CHECKLIST: *Order of attachments.*

4.1 Which documents are you submitting for review and approval with this CRR? *If new or updated documents are being submitted with this CRR, submit a completed Research Modification Form.*

4.1.a ☒ Protocol — Version: 7

4.1.b ☐ Protocol Synopsis — Version:

4.1.c ☒ Consent/Assent Form(s)

Consent/Assent Form #	Version	Description
Ext to 2015-Eng	2/10/10	Consent for the Extension Study
Ext to 2015-Span	5/1/10	Consent for the Extension Study
Long Life Study English	4/2/12	Consent for the Long Life Study
Long Life Study Spanish	5/17/12	Consent for the Long Life Study
Long Life Study Spanish	5/17/12	Consent for the Long Life Study

4.1.d ☐ Questionnaire(s)

Document Title	Version:
Form 33 & 33S – Medical History Update	11
Form 120 – Initial Notification of Death	V8.1
Form 125 – Summary of Hospitalization Diagnosis	8.1
Form 151 & 151S – Activities of Daily Life-English	9
Form 153 & 153S – Medication & Supplement Inventory	1
Form 155 & 155S – Lifestyle Questionnaire	1
Form 301 – In person Visit (LLS)	1
Form 321 & 321S – OPACH Physical Activity Questionnaire	1
AS340 Food Frequency Questionnaire for LLS English and Spanish	N/A

4.1.e ☐ Advertisements

Document Title	Version:

4.1.f ☐ Investigator's Brochure 🖇 Version:

4.1.g ☒ Any other documents, which are given to study participants or otherwise require IRB approval, that the study is currently using or will use in the next approval period (e.g., web pages, or internet-based collection tools) 🖇

Document Title	Version:
Extension Study Cover Letter contact 1 with Regional Center Listing template (English)	4
Extension Study Cover Letter contact 1 with Regional Center Listing template (Spanish)	4
Extension Study Cover Letter contact 2 with RC listing (English)	3
Extension Study Cover Letter contact 2 with RC listing (Spanish)	3
Medical Inventory Cover Letter – minor revision - English	5-2012
Medical Inventory Cover Letter – minor revision Spanish	5-2012
Medical Inventory Phone Script – minor revision English	5-2012
Medical Inventory Phone Script – minor revision Spanish	5-2012
WHI 2011 Annual Progress Report	2011

4.2 Order of Attachments. **Check all that apply:**

General Information

4.2.a *Per Question 1.6* Multi-Center Supplement ☒ Yes

4.2.b *Per Question 1.7* Funding Source Supplement ☒ Yes

4.2.c	*Per Question 1.8*	FHCRC Conflict of Interest Documents	☐ Yes
4.2.d	*Per Question 1.10*	Expedited Review Checklist for Minimal Risk Activities	☒ Yes

Ongoing Activities

4.2.e	*Per Question 2.3*	Research Modification Form	☒ Yes
4.2.f	*Per Question 2.4*	New research risk, findings, or other documentation	☐ Yes
4.2.g	*Per Question 2.4.f*	Independent safety monitoring committee and/or DSMB Minutes	☐ Yes
4.2.h	*Per Question 2.4.g*	PDMC Minutes	☐ Yes
4.2.i	*Per Question 2.7*	Expedited Reporting form – Continuing Noncompliance	☐ Yes
4.2.j	*Per Question 2.8.a*	Form FDA 483, sponsor or industry monitoring findings, Research Trials Office (RTO) monitoring reports	☐ Yes
4.2.k	*Per Question 2.11*	Repository Supplement	☐ Yes

5.0 INVESTIGATOR STATEMENT AND SIGNATURE

Study Title: Clinical Coordinating Center for the WHI Extension

As PRINCIPAL INVESTIGATOR, I acknowledge that all of the information provided in this CRR and the accompanying attachments is true to the best of my knowledge; that I am responsible for reporting any emergent problems, unanticipated problems involving risks to subjects or others, serious or continuing noncompliance, or proposed procedural modifications and that no modifications will be put into effect without prior Institutional Review Board (IRB) approval except where necessary to eliminate apparent immediate hazards; that unless otherwise directed by the IRB Chairperson, I will renew this research project with the IRB at the frequency specified in the IRB approval; that the research project is being conducted in compliance with the IRB's understanding and recommendations; that the IRB is provided all the information on the research project necessary for its complete review; and that this research project will not be put into effect until final IRB approval is received.

Janet Henderson
Signature of Investigator

June 6, 2012
Date

Ref: 102900 Date: 29Oct10 SHIP
Dep: Wgt: 0.2 LBS SF
DV: 0.00
Svcs: PRIORITY OVERNIGHT
TRCK: 432[illegible] 3738 0310

Wake Forest

FRED HUTCHINSON CANCER RESEARCH CENTER
Institutional Review Board

IRB Authorization Agreement

Institution A - Name of Institution or Organization Providing IRB Review:
Fred Hutchinson Cancer Research Center (FHCRC)

IRB Registration #: Com A (00000021), Com B (00000022), Com C (00005619)
Federalwide Assurance (FWA) #: FWA00001920

Institution B - Name of Institution Relying on the Designated IRB: **Wake Forest University Health Sciences, Medical Center Boulevard, Winston-Salem, NC 27157-1023**

Federalwide Assurance (FWA) #: FWA00001435

The Officials signing below agree that **Wake Forest University Health Sciences WHI Southeast Regional Center** may rely on the designated IRB for review and continuing oversight of its human subject research described below: (*check one*)

☐ This agreement applies to all human subject research covered by Fred Hutchinson Cancer Research Center's FWA.
☒ This agreement is limited to the following specific protocol(s):

Title of Research Project:	Human research activities of the WHI Regional/Satellite Center relating to "Clinical Coordinating Center for the WHI 2010-2015 Extension (FHCRC IRB #3467ext)"
FHCRC's Principal Investigator: Ross Prentice, PhD Garnet Anderson, PhD	Institution B's Principal Investigator: **Sally A. Shumaker, PHD**

The review performed by the designated IRB will meet the human subjects protection requirements of Institution B's OHRP-approved FWA. The IRB at Institution/Organization A will follow written procedures for reporting its findings and actions to appropriate officials at Institution B. Relevant minutes of IRB meetings will be made available to Institution B upon request. Institution B remains responsible for ensuring compliance with the IRB's determinations and with the Terms of its OHRP-approved FWA. The term of this Agreement shall be for a period of 5 (5) years, which term shall renew automatically for additional one-year periods unless terminated by either party upon thirty (30) days' advance written notice. This document must be kept on file at both institutions and provided to OHRP upon request.

Signatures:

Authorized Official of (A):

Karen Hansen 10/26/10
(signature) (date)
Name: Karen Hansen
Title: Director, Institutional Review Office

Mailing Address: 1100 Fairview Avenue N
Mailstop: J6-110
Seattle, WA 98109

Authorized Official of Institution (B) – Regional Center:

Joseph S. Andrews 9-28-10
(signature) (date)
Name: Joseph Andrews
Title: *IRB Director*

Mailing Address Office of Research
Medical Center Blvd.
Winston-Salem, NC 27157

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NCER RESEARCH CENTER

Tucson

Institutional Review Board

IRB Authorization Agreement

Institution A - Name of Institution or Organization Providing IRB Review:
Fred Hutchinson Cancer Research Center (FHCRC)

IRB Registration #: Com A (00000021), Com B (00000022), Com C (00005619)
Federalwide Assurance (FWA) #: FWA00001920

Institution B - Name of Institution Relying on the Designated IRB: ***University of Arizona, College of Public Health, Women's Health Initiative, Tucson, AZ***

Federalwide Assurance (FWA) #: ***FWA# 00004218, University of Arizona, Exp. 7/7/13***

The Officials signing below agree that **Tucson, AZ Satellite Center** may rely on the designated IRB for review and continuing oversight of its human subject research described below: (*check one*)

☐ This agreement applies to all human subject research covered by Fred Hutchinson Cancer Research Center's FWA.

☒ This agreement is limited to the following specific protocol(s):

Title of Research Project:	Human research activities of the WHI Regional/Satellite Center relating to "Clinical Coordinating Center for the WHI 2010-2015 Extension (FHCRC IRB #3467ext)"

FHCRC's Principal Investigator: Ross Prentice, PhD Garnet Anderson, PhD	Institution B's Principal Investigator: ***Dr. Cynthia Thomson***

The review performed by the designated IRB will meet the human subjects protection requirements of Institution B's OHRP-approved FWA. The IRB at Institution/Organization A will follow written procedures for reporting its findings and actions to appropriate officials at Institution B. Relevant minutes of IRB meetings will be made available to Institution B upon request. Institution B remains responsible for ensuring compliance with the IRB's determinations and with the Terms of its OHRP-approved FWA. The term of this Agreement shall be for a period of 5 (5) years, which term shall renew automatically for additional one-year periods unless terminated by either party upon thirty (30) days' advance written notice. This document must be kept on file at both institutions and provided to OHRP upon request.

Signatures:

Authorized Official of (A):

for Karen Hansen — 12-2-2010
(signature) (date)

Name: Karen Hansen
Title: Director, Institutional Review Office

Mailing Address: 1100 Fairview Avenue N
Mailstop: J6-110
Seattle, WA 98109

Phone: (206) 667-4867 Fax: (206) 667-6831
Email: khansen@fhcrc.org

Authorized Official of Institution (B) – Regional Center:

Leslie P. Tolbert — 11/22/10
(signature) (date)

Name: Leslie Tolbert, PhD
Title: Vice President, Research, Graduate Studies and Economic Development
Mailing Address Administration Bldg. 601
PO Box 210066
Tucson, AZ 85721-0066

Phone: (520) 621-3513 Fax: (520) 621-7507
Email: tolbert@email.arizona.edu

IRO REC'D JAN 05 2011

FRED HUTCHINSON
CANCER RESEARCH CENTER
Institutional Review Board

Stanford

IRB Authorization Agreement

Institution A - Name of Institution or Organization Providing IRB Review:
Fred Hutchinson Cancer Research Center (FHCRC)

IRB Registration #: Com A (00000021), Com B (00000022), Com C (00005619)
Federalwide Assurance (FWA) #: FWA00001920

Institution B - Name of Institution Relying on the Designated IRB:
Leland Stanford Junior U

Federalwide Assurance (FWA) #: FWA00000935

The Officials signing below agree that **Leland Stanford Junior U** may rely on the designated IRB for review and continuing oversight of its human subject research described below: (*check one*)

☐ This agreement applies to all human subject research covered by Fred Hutchinson Cancer Research Center's FWA.
☒ This agreement is limited to the following specific protocol(s):

Title of Research Project:	Human research activities of the WHI Regional/Satellite Center relating to "Clinical Coordinating Center for the WHI 2010-2015 Extension (FHCRC IRB #3467ext)"

FHCRC's Principal Investigator: Ross Prentice, PhD Garnet Anderson, PhD	Institution B's Principal Investigator: Marcia Stefanick, Ph.D.

The review performed by the designated IRB will meet the human subjects protection requirements of Institution B's OHRP-approved FWA. The IRB at Institution/Organization A will follow written procedures for reporting its findings and actions to appropriate officials at Institution B. Relevant minutes of IRB meetings will be made available to Institution B upon request. Institution B remains responsible for ensuring compliance with the IRB's determinations and with the Terms of its OHRP-approved FWA. The term of this Agreement shall be for a period of 5 (5) years, which term shall renew automatically for additional one-year periods unless terminated by either party upon thirty (30) days' advance written notice. This document must be kept on file at both institutions and provided to OHRP upon request.

Signatures:

Authorized Official of (A):

Karen Hansen 1/5/11
(signature) (date)
Name: Karen Hansen
Title: Director, Institutional Review Office

Mailing Address: 1100 Fairview Avenue N
Mailstop: J6-110
Seattle, WA 98109

Authorized Official of Institution (B) – Regional Center:

12/17/10
(signature) (date)
Name: Ann M. Arvin, M.D.
Title: Vice Provost and Dean of Research

Mailing Address: Office of the Dean of Research
Building 10, Main Quad
Stanford, CA 94305-2061

Phone: (206) 667-4867 Fax: (206) 667-6831 Phone: (650) 725-4421 Fax: (650) 725-1653
Email: khansen@fhcrc.org Email: aarvin@stanford.edu

IRO REC'D DEC 0 9 2010

Pittsburgh

FRED HUTCHINSON CANCER RESEARCH CENTER

di Institutional Review Board

IRB Authorization Agreement

Institution A - Name of Institution or Organization Providing IRB Review:
Fred Hutchinson Cancer Research Center (FHCRC)

IRB Registration #: Com A (00000021), Com B (00000022), Com C (00005619)
Federalwide Assurance (FWA) #: FWA00001920

Institution B - Name of Institution Relying on the Designated IRB: ***University of Pittsburgh***

Federalwide Assurance (FWA) #: *FWA00006790*

The Officials signing below agree that University of Pittsburgh may rely on the designated IRB for review and continuing oversight of its human subject research described below: (*check one*)

☐ This agreement applies to all human subject research covered by Fred Hutchinson Cancer Research Center's FWA.
☒ This agreement is limited to the following specific protocol(s):

Title of Research Project:	Human research activities of the WHI Regional/Satellite Center relating to "Clinical Coordinating Center for the WHI 2010-2015 Extension (FHCRC IRB #3467ext)"

FHCRC's Principal Investigator: Ross Prentice, PhD Garnet Anderson, PhD	Institution B's Principal Investigator: Lewis Kuller, MD

The review performed by the designated IRB will meet the human subjects protection requirements of Institution B's OHRP-approved FWA. The IRB at Institution/Organization A will follow written procedures for reporting its findings and actions to appropriate officials at Institution B. Relevant minutes of IRB meetings will be made available to Institution B upon request. Institution B remains responsible for ensuring compliance with the IRB's determinations and with the Terms of its OHRP-approved FWA. The term of this Agreement shall be for a period of 5 (5) years, which term shall renew automatically for additional one-year periods unless terminated by either party upon thirty (30) days' advance written notice. This document must be kept on file at both institutions and provided to OHRP upon request.

Signatures:

Authorized Official of (A):

for Karen Hansen 12-9-2010
(signature) (date)
Name: Karen Hansen
Title: Director, Institutional Review Office

Mailing Address: 1100 Fairview Avenue N
Mailstop: J6-110
Seattle, WA 98109

Phone: (206) 667-4867 Fax: (206) 667-6831
Email: khansen@fhcrc.org

Authorized Official of Institution (B) – Regional Center:

(signature) 11/23/10 (date)
Name: Randy P. Juhl, PhD
Title: Vice Chancellor for Research Conduct and Compliance

Mailing Address 132 Cathedral of Learning
4200 Fifth Avenue
Pittsburgh, PA 15260

Phone: 412-624-9111 Fax: 412-624-6903
Email: rjuhl@pitt.edu

MEDSTAR

IRO REC'D NOV 05 2010

FRED **HUTCHINSON**
CANCER RESEARCH **CENTER**
Institutional Review Board

IRB Authorization Agreement

Institution A - Name of Institution or Organization Providing IRB Review: **Fred Hutchinson Cancer Research Center (FHCRC)**
IRB Registration #: Com A (00000021), Com B (00000022), Com C (00005619)
Federalwide Assurance (FWA) #: FWA00001920

Institution B - Name of Institution Relying on the Designated IRB: **MedStar Health Research Institute**

Federalwide Assurance (FWA) #: FWA00000504

The Officials signing below agree that **MedStar Health Research Institute** may rely on the designated IRB for review and continuing oversight of its human subject research described below: (*check one*)

☐ This agreement applies to all human subject research covered by Fred Hutchinson Cancer Research Center's FWA.

☒ This agreement is limited to the following specific protocol(s):

Title of Research Project:	Human research activities of the WHI Regional/Satellite Center relating to "Clinical Coordinating Center for the WHI 2010-2015 Extension (FHCRC IRB #3467EXT)"
FHCRC Principal Investigator: Ross Prentice, PhD Garnet Anderson, PhD	Institution B's Principal Investigator: Barbara Howard, PhD

The review performed by the designated IRB will meet the human subjects protection requirements of Institution B's OHRP-approved FWA. The IRB at Institution/Organization A will follow written procedures for reporting its findings and actions to appropriate officials at Institution B. Relevant minutes of IRB meetings will be made available to Institution B upon request. Institution B remains responsible for ensuring compliance with the IRB's determinations and with the Terms of its OHRP-approved FWA. The term of this Agreement shall be for a period of five (5) years, which term shall renew automatically for additional one-year periods unless terminated by either party upon thirty (30) days' advance written notice. This document must be kept on file at both institutions and provided to OHRP upon request.

Signatures:

Authorized Official of (A):

Karen Hansen 11/5/10
(signature) *(date)*

Name: Karen Hansen
Title: Director, Institutional Review Office

Mailing Address: 1100 Fairview Avenue N
Mailstop: J6-110
Seattle, WA 98109

Phone: (206) 667-4867 *Fax*: (206) 667-6831
Email: khansen@fhcrc.org

Authorized Official of (B) MedStar Health Research Institute:

(signature) 11-4-10 *(date)*

Name: William Thomas
Title: Executive VP for Medical Affairs

Mailing Address 5565 Sterrett Place, 5th flr
Columbia, MD 21044

Phone: 410-772-6544 *Fax*: 410-772-6543
Email: William.l.thomas@medstar.net

Iowa

FRED HUTCHINSON
CANCER RESEARCH CENTER
Institutional Review Board

IRB Authorization Agreement

Institution A - Name of Institution or Organization Providing IRB Review:
Fred Hutchinson Cancer Research Center (FHCRC)

IRB Registration #: Com A (00000021), Com B (00000022), Com C (00005619)
Federalwide Assurance (FWA) #: FWA00001920

Institution B - Name of Institution Relying on the Designated IRB: ***The University of Iowa***

Federalwide Assurance (FWA) #: FWA00003007

The Officials signing below agree that **The University of Iowa IRB** may rely on the designated IRB for review and continuing oversight of its human subject research described below: (*check one*)

☐ This agreement applies to all human subject research covered by Fred Hutchinson Cancer Research Center's FWA.
☒ This agreement is limited to the following specific protocol(s):

Title of Research Project:	Human research activities of the WHI Regional/Satellite Center relating to "Clinical Coordinating Center for the WHI 2010-2015 Extension (FHCRC IRB #3467ext)"

FHCRC's Principal Investigator:	Institution B's Principal Investigator:
Ross Prentice, PhD Garnet Anderson, PhD	Robert Wallace, MD Jennifer Robinson, MD, MPH

The review performed by the designated IRB will meet the human subjects protection requirements of Institution B's OHRP-approved FWA. The IRB at Institution/Organization A will follow written procedures for reporting its findings and actions to appropriate officials at Institution B. Relevant minutes of IRB meetings will be made available to Institution B upon request. Institution B remains responsible for ensuring compliance with the IRB's determinations and with the Terms of its OHRP-approved FWA. The term of this Agreement shall be for a period of 5 (5) years, which term shall renew automatically for additional one-year periods unless terminated by either party upon thirty (30) days' advance written notice. This document must be kept on file at both institutions and provided to OHRP upon request.

Signatures:

Authorized Official of (A):

Karen Hansen 10/19/10
(signature) (date)
Name: Karen Hansen
Title: Director, Institutional Review Office

Mailing Address: 1100 Fairview Avenue N
Mailstop: J6-110
Seattle, WA 98109

Phone: (206) 667-4867 Fax: (206) 667-6831
Email: khansen@fhcrc.org

Authorized Official of Institution (B) – Regional Center:

James C Walker 9/24/2010
(signature) (date)
Name: James C. Walker
Title: Executive Associate Vice President

Mailing Address The University of Iowa
201 Gilmore Hall
Iowa City, IA 52242

Phone: 319 335 9546 Fax:
Email: james-walker@uiowa.edu

IRB REC'D OCT 25 2010

Gainesville

FRED HUTCHINSON
CANCER RESEARCH CENTER
Institutional Review Board

IRB Authorization Agreement

Institution A - Name of Institution or Organization Providing IRB Review:
Fred Hutchinson Cancer Research Center (FHCRC)

IRB Registration #: Com A (00000021), Com B (00000022), Com C (00005619)
Federalwide Assurance (FWA) #: FWA00001920

Institution B - Name of Institution Relying on the Designated IRB: ***<<University of Florida***

Federalwide Assurance (FWA) #: <<FWA00005790 >>

The Officials signing below agree that **<<University of Florida>>** may rely on the designated IRB for review and continuing oversight of its human subject research described below: (*check one*)

☐ This agreement applies to all human subject research covered by Fred Hutchinson Cancer Research Center's FWA.
☒ This agreement is limited to the following specific protocol(s):

Title of Research Project:	Human research activities of the WHI Regional/Satellite Center relating to "Clinical Coordinating Center for the WHI 2010-2015 Extension (FHCRC IRB #3467ext)"

FHCRC's Principal Investigator:	Institution B's Principal Investigator:
Ross Prentice, PhD Garnet Anderson, PhD	Marian Limacher, MD

The review performed by the designated IRB will meet the human subjects protection requirements of Institution B's OHRP-approved FWA. The IRB at Institution/Organization A will follow written procedures for reporting its findings and actions to appropriate officials at Institution B. Relevant minutes of IRB meetings will be made available to Institution B upon request.

Institution A agrees to notify Institution B as follows:

- Immediately:
  - Any termination or suspension of IRB approval (including suspension of enrollment).
  - Upon completion, any audit or investigation findings related to Institution B's conduct of the study.

- Promptly:
  - Any subject complaints related to Institution B's conduct of the study;
  - Any serious or continuing non-compliance related to Institution B's conduct of the study;
  - Any unanticipated problems related to Institutions B's conduct of the study; and
  - Any findings from outside regulatory agencies related to Institution B's conduct of the study

Institution B remains responsible for ensuring compliance with the IRB's determinations and with the Terms of its OHRP-approved FWA. The term of this Agreement shall be for a period of five (5) years, which term shall renew automatically for additional one-year periods unless terminated by either party upon thirty (30) days' advance written notice. This document must be kept on file at both institutions and provided to OHRP upon request.

Signatures:

Authorized Official of (A):

Karen Hansen 10/26/10
(signature) (date)

Name: Karen Hansen
Title: Director, Institutional Review Office

Mailing Address: 1100 Fairview Avenue N
Mailstop: J6-110
Seattle, WA 98109

Phone: (206) 667-4867 Fax: (206) 667-6831
Email: khansen@fhcrc.org

Authorized Official of Institution (B) – Regional Center:

Winfred M. Phillips 10/19/10
(signature) (date)

Name: Winfred M. Phillips, D.Sc.
Title: Vice President for Research

Mailing Address: PO Box 115500
Gainesville, FL 32611

Phone: 352-392-9271 Fax: 352-846-0491
Email: wphil@ufl.edu

Institutional Review Board (IRB) Authorization Agreement

Name of Institution Providing IRB Review: Fred Hutchinson Cancer Research Center

IRB Registration #: Com A (00000021), Com B (00000022), Com C (00005619)
Federalwide Assurance #: FWA00001920

Name of Organization Relying on the Designated IRB: Ohio State University

Federalwide Assurance #: FWA00006378

The Officials signing below agree that Ohio State University may rely on the designated IRB for review and continuing oversight of its human subjects research described below:

This agreement is limited to the following specific protocol(s):

Name of Research Project: Human research activities of the WHI Regional/Satellite Center relating to "Clinical Coordinating Center for the WHI 2010-2015 Extension (FHCRC IRB #3467ext)"

Ohio State University Principal Investigator: Rebecca D. Jackson, MD
Ohio State University Point of Contact: Judith Neidig, PhD, Phone: 614-292-1840, Fax: 614-688-0366, Email: neidig.1@osu.edu

Fred Hutchinson Cancer Research Center Principal Investigator: Ross Prentice, PhD & Garnet Anderson, PhD
Fred Hutchinson Cancer Research Center Point of Contact: Karen Hansen, Phone: 206-667-4867, Fax: 206-667-6831, Email: khansen@fhcrc.org

Funding Agency: National Institutes of Health

The review performed by the Fred Hutchinson Cancer Research Center IRB will meet the human subject protection requirements of The Ohio State University's OHRP-approved FWA. The IRB at the Fred Hutchinson Cancer Research Center will follow standard procedures for reporting its findings and actions to appropriate officials at The Ohio State University. Relevant minutes of IRB meetings will be made available to The Ohio State University upon request. Subject complaints, serious and/or continuing non-compliance, IRB suspension or termination of research and unanticipated problems involving risks to subjects or others will be reported to The Ohio State University's IRB within 30 days of IRB review. The Ohio State University remains responsible for ensuring compliance with the IRB's determinations and with the Terms of its OHRP-approved FWA. This document must be kept on file by both parties and provided to ORHP upon request.

Signature of Signatory Official of the Fred Hutchinson Cancer Research Center:

Karen Hansen _____ **Date:** 11/10/10

Karen Hansen
Director, Institutional Review office
Fred Hutchinson Cancer Research Center
1100 Fairview Avenue N
Mailstop: J6-110
Seattle, WA 98109
Phone: (206) 667-4867 Fax: (206) 667-6831
Email: khansen@fhcrc.org

Signature of Signatory Official of the Ohio State University:

Date: 11/4/10

Janet M. Weisenberger, PhD
Senior Associate Vice President for Research
Ohio State University
190 N Oval Mall, Room 208
Columbus, OH 43210
Phone: (614) 292-1582 Fax: (614) 292-6602
Email: weisenberger.21@osu.edu

In deferring the University's Federalwide Assurance and Institutional Review Board review to the Fred Hutchinson Cancer Research Center, the College of Medicine and its Department of Internal Medicine agree to be responsible for the Fred Hutchinson Cancer Research Center's use of human subjects in research conducted under this Agreement.

(Signature) 10/15/10 (Date)

Brad Rovin, MD
Vice Chair of Research, Department of Internal Medicine

(Signature) 10/18/10 (Date)

Clay Marsh, MD
Vice Dean for Research, College of Medicine

Buffalo IRO REC'D NOV 0 2 2010

FRED HUTCHINSON CANCER RESEARCH CENTER
Institutional Review Board

IRB Authorization Agreement

Institution A - Name of Institution or Organization Providing IRB Review:
Fred Hutchinson Cancer Research Center (FHCRC)

IRB Registration #: Com A (00000021), Com B (00000022), Com C (00005619)
Federalwide Assurance (FWA) #: FWA00001920

Institution B - Name of Institution Relying on the Designated IRB: ***University at Buffalo***

Federalwide Assurance (FWA) #: ***FWA00008824***

The Officials signing below agree that **<<insert name of regional/satellite center>>** may rely on the designated IRB for review and continuing oversight of its human subject research described below: *(check one)*

☐ This agreement applies to all human subject research covered by Fred Hutchinson Cancer Research Center's FWA.
☒ This agreement is limited to the following specific protocol(s):

Title of Research Project:	Human research activities of the WHI Regional/Satellite Center relating to "Clinical Coordinating Center for the WHI 2010-2015 Extension (FHCRC IRB #3467ext)"

FHCRC's Principal Investigator:	Institution B's Principal Investigator:
Ross Prentice, PhD Garnet Anderson, PhD	***Jean Wactawski-Wende, PhD***

The review performed by the designated IRB will meet the human subjects protection requirements of Institution B's OHRP-approved FWA. The IRB at Institution/Organization A will follow written procedures for reporting its findings and actions to appropriate officials at Institution B. Relevant minutes of IRB meetings will be made available to Institution B upon request. Institution B remains responsible for ensuring compliance with the IRB's determinations and with the Terms of its OHRP-approved FWA. The term of this Agreement shall be for a period of 5 (5) years, which term shall renew automatically for additional one-year periods unless terminated by either party upon thirty (30) days' advance written notice. This document must be kept on file at both institutions and provided to OHRP upon request.

Signatures:

Authorized Official of (A):
Karen Hansen (KH) 11/3/10
(signature) (date)
Name: Karen Hansen
Title: Director, Institutional Review Office

Mailing Address: 1100 Fairview Avenue N
Mailstop: J6-110
Seattle, WA 98109

Phone: (206) 667-4867 Fax: (206) 667-6831
Email: khansen@fhcrc.org

Authorized Official of Institution (B) – Regional Center:
Alexander Cartwright 11/2/10
(signature) (date)
Name: **Alexander N. Cartwright, PhD**
Title: **VP Research, Professor**

Mailing Address **516 Capen Hall**
University at Buffalo
Buffalo, NY 14260-1631

Phone: **716-645-3321** Fax: **716-645-6792**
Email: **vpr@buffalo.edu**

Boston

Institutional Review Board (IRB) Authorization Agreement

Name of Institution Providing IRB Review:

FRED HUTCHINSON CANCER RESEARCH CENTER (FHCRC) - Federalwide Assurance (FWA) # 00001920 – IRB Registration # Com A (00000021), Com B (00000022), Com C (00005619)

Name of Institution Relying on the Designated IRB:

BRIGHAM AND WOMEN'S HOSPITAL (BWH) - Federalwide Assurance (FWA) # 00000484

Terms of Agreement

1. The Officials signing below agree that BWH, a member institution of Partners HealthCare System, Inc. (PARTNERS), may rely on the FHCRC IRB for review and continuing oversight of its human subject research described below:

   Name of Research Project: **Women's Health Initiative (WHI) Extension Study**
   Protocol #: **FHCRC IRB #3467EXT**
   Name(s) of Principal Investigator(s) at each Site: **Ross Prentice, PhD & Garnet Anderson, PhD (FHCRC)**
   Joann Manson, MD, Dr PH (BWH)
   Sponsor or Funding Source and Award # (if any): **Research Foundation of State University of New York**

2. The review and continuing oversight performed by the FHCRC IRB will meet the human subjects protection requirements of BWH's OHRP-approved FWA, a copy of which is available to the FHCRC IRB.

3. The FHCRC IRB will perform any determination required by the Health Insurance Portability and Accountability Act (HIPAA) and its regulations with respect to the research included under this Agreement, including determinations related to waivers of authorization for use and disclosure for research of subjects' Protected Health Information (PHI) as defined in the HIPAA regulations. FHCRC will provide a form of authorization for use and disclosure of PHI if such authorization is required. Determinations as to the legal sufficiency of such authorization forms under HIPAA shall be made by the entity or organization from which PHI is obtained for the research.

4. The FHCRC IRB will allow representatives of BWH to attend its meetings and will otherwise accept comments from BWH's representatives in the review of study, to the extent necessary to ensure sufficient knowledge of the local research context.

5. The FHCRC IRB, or the Women's Health Initiative CCC, will notify BWH and the responsible BWH PI in writing of its decision to approve or disapprove the study or of modifications required to secure approval of the study, as well as subsequent IRB-reviewed and approved changes in the research activity, namely, by sending copies to the BWH officials designated in this Agreement and to the BWH PI of the review notification letters it sends to investigators. Relevant minutes of FHCRC IRB meetings pertaining to the study will be made available to BWH upon written request.

6. BWH remains responsible in connection with the study for ensuring compliance with the determinations of the FHCRC IRB and with the terms of BWH's OHRP-approved FWA.

7. The FHCRC IRB will promptly notify BWH in writing of any serious or continuing non-compliance by BWH or its investigators discovered by the FHCRC IRB or FHCRC, any suspension or termination of IRB approval, and any injuries to subjects or unanticipated problems involving risks to subjects or others discovered by the FHCRC IRB or FHCRC in connection with the study. BWH will promptly report to

FHCRC any serious or continuing non-compliance by BWH or its investigators in connection with the study of which it is aware, and will make all reasonable efforts to ensure that its investigators promptly report to FHCRC any injury to subjects or unanticipated problem involving risks to subjects or others in connection with the study of which they are aware.

8. FHCRC will be responsible for any investigation of non-compliance or other such matters. If the investigative process includes the production of a report that will be made externally (e.g. OHRP), FHCRC shall provide a copy of such report made to external organizations. Nothing in this Agreement shall prevent BWH from conducting its own inquiry or investigation into any such matter pursuant to its own policies and procedures, or from making its own report to external authorities, or from taking additional, more restrictive remediation steps at its own institution, including the termination of participation by BWH investigators in the study. Each party agrees to use all reasonable efforts to cooperate with one another's inquiries or investigations, including providing access to necessary research records and related information and meeting with research representatives upon request.

9. This Agreement shall become effective on the last date signed below and shall continue until completion of the research as determined by the FHCRC IRB, provided that the parties' FWAs remain in good standing and provided that the Agreement is not earlier terminated as provided in Section 11 below.

10. Either FHCRC or BWH may terminate this Agreement (i) without cause upon 30 days prior written notice to the other or (ii) upon 14 days prior written notice to the other in the event of a breach by the other that is not cured to the reasonable satisfaction of the non-breaching party within said 14-day notice period. In the event of any termination, the parties will ensure that OHRP is notified and will work together to determine effect of such termination on the research being conducted under the Agreement at the time of termination. Sections 8, 9, 11, and 12 of this Agreement will survive any expiration or termination of the Agreement.

11. All communications, reports and notices required under this Agreement shall be delivered by hand, by facsimile, or by first-class mail, postage prepaid and addressed as follows:

If to BWH/Partners:
P. Pearl O'Rourke, M.D.
Director of Human Research Affairs
Partners HealthCare System, Inc.
Research Management
116 Huntington Ave., Suite 1002
Boston, MA 02116
Fax: (617) 424-4199

With copies to:
Elizabeth L. Hohmann, M.D.
Director and Chair
Partners Human Research Committee
116 Huntington Ave., Suite 1002
Boston, MA 02116
Fax: (617) 424-4199

and:
Maria Sundquist
Assistant Director, New Submissions
Partners Human Research Committee
116 Huntington Ave., Suite 1002
Boston, MA 02116
Fax: (617) 424-4199
Email: msundquist@partners.org

If to FHCRC:

Karen Hansen
Director, Institutional Review Office
Fred Hutchinson Cancer Research Center
1100 Fairview Avenue N – Mailstop J6-110
Seattle, WA 98109
Fax: (206) 667-6831
Email khansen@fhcrc.org

12. Miscellaneous: This Agreement has been executed and delivered in and shall be governed by and construed and interpreted in accordance with the laws of the Commonwealth of Massachusetts. This Agreement may be amended only by a written agreement signed by the parties. If any provision of this Agreement shall be held to be invalid, illegal, or unenforceable, the validity, legality and enforceability of the remaining provisions of this Agreement shall not be affected thereby. The failure of a party to insist upon the strict performance of any of the terms of this Agreement shall not be construed to be a waiver or relinquishment of any of the terms of the Agreement or of the whole Agreement. This Agreement is not assignable in whole or in part, and any attempt to do so shall be void.

This Agreement must be kept on file at both institutions and provided to OHRP upon request.

EXECUTED BY AUTHORIZED SIGNATORY OFFICIALS

P. Pearl O'Rourke Date: 11/22/11

Name: P. Pearl O'Rourke, M.D.
Institutional Title: Director of Human Research Affairs
Partners HealthCare System, Inc.
Research Management
116 Huntington Ave., Suite 1002
Boston, MA 02116

Barbara E. Bierer Date: 11/18/2011

Name: Barbara E. Bierer, MD
Institutional Title: Senior Vice President, Research
Brigham and Women's Hospital
75 Francis Street -- PB-04-415
Boston, MA 02115

Karen Hansen Date: 10/14/11

Name: Karen Hansen
Institutional Title: Director, Institutional Review Office
Fred Hutchinson Cancer Research Center
1100 Fairview Avenue N – Mailstop J6-110
Seattle, WA 98109